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* * * * * * * * * *  Welcome to STN International  * * * * * * * *
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 NEWS 1       Web Page URLs for STN Seminar Schedule - N.
America
 NEWS 2       "Ask CAS" for self-help around the clock
 NEWS 3  May 12  EXTEND option available in structure searching
 NEWS 4  May 12  Polymer links for the POLYLINK command
completed in REGISTRY
 NEWS 5  May 27  New UPM (Update Code Maximum) field for more
efficient patent
          SDIs in CAplus
 NEWS 6  May 27  CAplus super roles and document types
searchable in REGISTRY
 NEWS 7  Jun 28  Additional enzyme-catalyzed reactions added to
CASREACT
 NEWS 8  Jun 28  ANTE, AQUALINE, BIOENG, CIVILENG,
ENVIROENG, MECHENG,
          and WATER from CSA now available on STN(R)
 NEWS 9  Jul 12  BEILSTEIN enhanced with new display and select
options,
          resulting in a closer connection to BABS
 NEWS 10 Jul 30  BEILSTEIN on STN workshop to be held August
24 in conjunction
          with the 228th ACS National Meeting
 NEWS 11 AUG 02  IFIPAT/IFIUDB/IFICDB reloaded with new
search and display
          fields
 NEWS 12 AUG 02  CAplus and CA patent records enhanced with
European and Japan
          Patent Office Classifications
 NEWS 13 AUG 02  STN User Update to be held August 22 in
conjunction with the
          228th ACS National Meeting
 NEWS 14 AUG 02  The Analysis Edition of STN Express with
Discover!
          (Version 7.01 for Windows) now available
 NEWS 15 AUG 04  Pricing for the Save Answers for SciFinder
Wizard within
          STN Express with Discover! will change September 1,
2004
 NEWS 16 AUG 27  BIOCOMMERCE: Changes and enhancements to
content coverage
 NEWS 17 AUG 27  BIOTECHABS/BIOTECHDS: Two new display
fields added for legal
          status data from INPADOC
 NEWS 18 SEP 01  INPADOC: New family current-awareness alert
(SDI) available
 NEWS 19 SEP 01  New pricing for the Save Answers for SciFinder
Wizard within
          STN Express with Discover!
 NEWS 20 SEP 01  New display format, HITSTR, available in
WPIDS/WPINDEX/WPIX

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01,
CURRENT
          MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
          AND CURRENT DISCOVER FILE IS DATED 11 AUGUST
2004
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                                          ENTRY   SESSION
FULL ESTIMATED COST                          0.21      0.21

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FILE COVERS 1907 - 7 Sep 2004  VOL 141 ISS 11
FILE LAST UPDATED: 6 Sep 2004  (20040906/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s (suc1(w)associated(w)neurotrophic(w)factor#)/bi,ab
         173 SUC1/BI
         121 SUC1/AB
      104087 ASSOCIATED/BI
        9949 ASSOCIATED/AB
       13132 NEUROTROPHIC/BI
        8316 NEUROTROPHIC/AB
     1363480 FACTOR#/BI
     1133791 FACTOR#/AB
L1         2
(SUC1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB

=> s snt?bi,ab
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'SNT?BI'
The truncation symbol ?  may be used only at the end of a search
term.  To specify a variable character within a word use '!', e.g.,
'wom!n' to search for both 'woman' and 'women'.  Enter "HELP
TRUNCATION" at an arrow prompt (=>) for more information.

=> s snt/bi,ab
         139 SNT/BI
         119 SNT/AB
L2       139 SNT/BI,AB

=> s (suc(w)1(w)associated(w)neurotrophic(w)factor#)/bi,ab
```

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      1247 SUC/BI
      1209 SUC/AB
   8000722 1/BI
   7320245 1/AB
    104087 ASSOCIATED/BI
      9949 ASSOCIATED/AB
     13132 NEUROTROPHIC/BI
      8316 NEUROTROPHIC/AB
   1363480 FACTOR#/BI
   1133791 FACTOR#/AB
L3         0
(SUC(W)1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB

=> d his

    (FILE 'HOME' ENTERED AT 14:38:03 ON 07 SEP 2004)

    FILE 'CAPLUS' ENTERED AT 14:38:12 ON 07 SEP 2004
L1           2 S
(SUC1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB
L2         139 S SNT/BI,AB
L3           0 S
(SUC(W)1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB

=> s l1 or l2 or l3
L4         139 L1 OR L2 OR L3

=> s (fibroblast(w)growth(w)factor(w)receptor#)/bi,ab
     77998 FIBROBLAST/BI
     36123 FIBROBLAST/AB
   1139144 GROWTH/BI
    948134 GROWTH/AB
    850698 FACTOR/BI
    705520 FACTOR/AB
    677772 RECEPTOR#/BI
    577410 RECEPTOR#/AB
L5        3240
(FIBROBLAST(W)GROWTH(W)FACTOR(W)RECEPTOR#)/BI,AB

=> s fgfr/bi,ab
      1018 FGFR/BI
       955 FGFR/AB
L6        1018 FGFR/BI,AB

=> s l5 or l6
L7        3397 L5 OR L6

=> s l4 and l7
L8          16 L4 AND L7

=> d his

    (FILE 'HOME' ENTERED AT 14:38:03 ON 07 SEP 2004)

    FILE 'CAPLUS' ENTERED AT 14:38:12 ON 07 SEP 2004
L1           2 S
(SUC1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB
L2         139 S SNT/BI,AB
L3           0 S
(SUC(W)1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB
L4         139 S L1 OR L2 OR L3
L5        3240 S
(FIBROBLAST(W)GROWTH(W)FACTOR(W)RECEPTOR#)/BI,AB
L6        1018 S FGFR/BI,AB
L7        3397 S L5 OR L6
L8          16 S L4 AND L7

=> d l8 1-16 bib ab

L8  ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2004 ACS on STN
AN  2004:396054  CAPLUS Full-text
DN  141:65396
TI  Tyrosine phosphorylation of sprouty proteins regulates their
ability to
    inhibit growth factor signaling: A dual feedback loop
AU  Mason, Jacqueline M.; Morrison, Debra J.; Bassit, Bhramdeo;
Dimri,
    Manjari; Band, Hamid; Licht, Jonathan D.; Gross, Isabelle
CS  Division of Hematology/Oncology, Department of Medicine,
Mount Sinai
    School of Medicine, New York, NY, 10029, USA
SO  Molecular Biology of the Cell (2004), 15(5), 2176-2188
    CODEN: MBCEEV; ISSN: 1059-1524
PB  American Society for Cell Biology
DT  Journal
LA  English
AB      Sprouty proteins are recently identified receptor tyrosine
        kinase (RTK) inhibitors potentially involved in many
        developmental processes. Here, the authors report that
        Sprouty proteins become tyrosine phosphorylated after
        growth factor treatment. The authors identified Tyr 55 as
        a key residue for Sprouty2 phosphorylation and showed
        that phosphorylation was required for Sprouty2 to inhibit
        RTK signaling, because a mutant Sprouty2 lacking Tyr 55
        augmented signaling. The authors found that tyrosine
        phosphorylation of Sprouty2 affected neither its subcellular
        localization nor its interaction with Grb2, FRS2/SNT, or
        other Sprouty proteins. In contrast, Sprouty2 tyrosine
        phosphorylation was necessary for its binding to the Src
        homol. 2-like domain of c-Cb1 after fibroblast growth factor
        (FGF) stimulation. To determine whether c-Cb1 was
        required for Sprouty2-dependent cellular events, Sprouty2
        was introduced into c-Cb1-wild-type and -null fibroblasts.
        Sprouty2 efficiently inhibited FGF-induced phosphorylation
        of extracellular signal-regulated kinase 1/2 in c-Cb1-null
        fibroblasts, thus indicating that the FGF-dependent binding
        of c-Cb1 to Sprouty2 was dispensable for its inhibitory
        activity. However, c-Cb1 mediates
        polyubiquitylation/proteasomal degradation of Sprouty2 in
        response to FGF. Last, using Src-family pharmacol.
        inhibitors and dominant-neg. Src, the authors showed that
        a Src-like kinase was required for tyrosine phosphorylation
        of Sprouty2 by growth factors. Thus, these data highlight
        a novel neg. and pos. regulatory loop that allows for the
        controlled, homeostatic inhibition of RTK signaling.
RE.CNT  47  THERE ARE 47 CITED REFERENCES AVAILABLE FOR
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        ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8  ANSWER 2 OF 16  CAPLUS  COPYRIGHT 2004 ACS on STN
AN  2004:219931  CAPLUS Full-text
DN  140:248186
TI  Use of patterns of gene expression to identify tissue types and
in disease
    diagnosis and prognosis
IN  Glinskii, Guennadi V.
PA  Sidney Kimmel Cancer Center, USA
SO  U.S. Pat. Appl. Publ., 209 pp., which which which which
    CODEN: USXXCO
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.          KIND  DATE       APPLICATION NO.
DATE
    ----------          ----  --------   --------------------  --------
PI  US 2004053317       A1    20040318   US 2003-660434
20030910
    WO 2004025258       A2    20040325   WO 2003-US28707
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20030910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-410018P P 20020910
US 2002-411155P P 20020916
US 2002-429168P P 20021125
US 2003-444348P P 20030131
US 2003-460826P P 20030403

AB Methods of using quant. anal. of array hybridizations to identify normal and diseased tissue in the diagnosis and prognosis of disease are described. The methods segregate individual samples into distinct classes using quant. measurements of expression values for selected sets of genes in individual samples compared to a reference standard Samples displaying pos. and neg. correlations of the gene expression values with the reference standard samples exhibit distinct behaviors and pathohistol. features. Also disclosed are methods for identifying sets of genes whose expression patterns are correlated with a phenotype. Such sets are useful for characterizing cellular differentiation pathways and states and for identifying potential drug discovery targets. Panels for diagnosis and determination of risk of invasive and metastatic forms of lung, prostate and breast cancer are identified. Similarly, panels indicating recurrence of the cancers and poor prognostic outcomes are identified.

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:809939 CAPLUS Full-text
DN 138:83646
TI mSprouty2 inhibits FGF10-activated MAP kinase by differentially binding to
upstream target proteins
AU Tefft, D.; Lee, M.; Smith, S.; Crowe, D. L.; Bellusci, S.; Warburton, D.
CS Center for Craniofacial Biology, Departments of Surgery and Pediatrics,
The Childrens Hospital Los Angeles Research Institute, University of
Southern California Schools of Dentistry and Medicine, Los Angeles, CA,
90023, USA
SO American Journal of Physiology (2002), 283(4, Pt. 1), L700-L706
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English

AB Murine Sprouty2 (mSpry2) is a conserved ortholog of Drosophila Sprouty, a gene that inhibits several tyrosine kinase receptor pathways, resulting in net reduction of mitogen-activated protein (MAP) kinase activation. However, the precise mechanism mediating mSpry2 function as a neg. regulator in tyrosine kinase growth factor pathways that regulate diverse biol. functions remains incompletely characterized. Fibroblast growth factor 10 (FGF10) is a key pos. regulator of lung branching morphogenesis and induces epithelial expression of mSpry2 adjacent to mesenchymal sites of FGF10. Herein, we demonstrate that FGF10 stimulation of mouse lung epithelial cells (MLE15) overexpressing mSpry2 results in both mSpry2 tyrosine phosphorylation and differential binding of mSpry2 to several key upstream target proteins in the MAP kinase-activating pathway. Thus FGF receptor (**FGFR**) activation results in increased association of mSpry2 with growth factor receptor-binding protein 2, suc-1-associated neurotrophic factor target 2, and Raf but decreased binding to protein tyrosine phosphatase 2 and GTPase-activating protein 1, resulting in a net reduction of MAP kinase activation. MSpry2 also spatially translocates to the plasma membrane and intracellular membrane structures in response to FGF10 stimulation. Our data demonstrate novel intracellular mechanisms mediating mSpry2 function as a neg. regulator of uncontrolled FGF-induced MAP kinase signaling.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:441726 CAPLUS Full-text
DN 137:166468
TI The molecular basis of Src kinase specificity during vertebrate mesoderm
formation
AU Hama, Joanne; Suri, Crystal; Haremaki, Tomomi; Weinstein, Daniel C.
CS Department of Pharmacology and Biological Chemistry, Mount Sinai School of
Medicine, New York, NY, 10029, USA
SO Journal of Biological Chemistry (2002), 277(22), 19806-19810
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English

AB Members of the Src family of non-receptor tyrosine kinases play a crit. role in mesoderm formation in the frog, Xenopus laevis, acting as required mediators downstream of the **fibroblast growth factor receptor.** At least 4 members of this gene family, Src, Fyn, Yes, and Laloo, are expressed during early embryonic development. Ectopic expression of Laloo and Fyn, but not Src, induce mesoderm in ectodermal explants, indicating that these factors are non-redundant during early vertebrate development. Here we investigate the basis for the differential activity of the Src and Laloo kinases during mesoderm formation. Although both Src and Laloo phys. interact with the substrate protein **SNT**-1/FRS2α only Laloo phosphorylates **SNT**-1, an event previously shown to be required for the activity of the latter and for mesoderm induction in vivo. Src is enzymically capable of stimulating mesoderm formation, as an activated Src construct both phosphorylates **SNT**-1 and induces mesoderm in explant cultures. However, a chimeric Laloo construct containing a Src C-terminal tail is inactive, suggesting that the early embryo contains a specific Laloo-activating, or Src-inactivating, factor. Finally, through further chimeric anal., we provide evidence to suggest that differences in Laloo

and Src activity are also mediated by the SH2, SH3, and kinase domains of these mols.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:371299 CAPLUS Full-text
DN 137:88559
TI FRS2 PTB domain conformation regulates interactions with divergent
neurotrophic receptors
AU Yan, Kelley S.; Kuti, Miklos; Yan, Sherry; Mujtaba, Shiraz; Farooq, Amjad;
Goldfarb, Mitchell P.; Zhou, Ming-Ming
CS Structural Biology Program, Department of Physiology and Biophysics, Mount
Sinai School of Medicine, New York University, New York, NY, 10029, USA
SO Journal of Biological Chemistry (2002), 277(19), 17088-17094
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Membrane-anchored adaptor proteins FRS2α/β (also known as **SNT**-1/2) mediate signaling of **fibroblast growth factor receptors** (FGFRs) and neurotrophin receptors (TRKs) through their N-terminal phosphotyrosine binding (PTB) domains. The FRS2 PTB domain recognizes tyrosine-phosphorylated TRKs at an NPXpY (where pY is phosphotyrosine) motif, whereas its constitutive association with **FGFR** involves a receptor juxtamembrane region lacking Tyr and Asn residues. Here we show by isothermal titration calorimetry that the FRS2α PTB domain binding to peptides derived from TRKs or **FGFR** is thermodynamically different. TRK binding is largely enthalpy-driven, whereas the **FGFR** interaction is governed by a favorable entropic contribution to the free energy of binding. Furthermore, our NMR spectral anal. suggests that disruption of an unstructured region C-terminal to the PTB domain alters local conformation and dynamics of the residues at the ligand-binding site, and that structural disruption of the β8-strand directly weakens the PTB domain association with the **FGFR** ligand. Together, our new findings support a mol. mechanism by which conformational dynamics of the FRS2α PTB domain dictates its association with either fibroblast growth factor or neurotrophin receptors in neuronal development.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:145800 CAPLUS Full-text
DN 136:337951
TI Docking protein SNT1 is a critical mediator of fibroblast growth factor
signaling during Xenopus embryonic development
AU Akagi, Keiko; Park, Eui Kyun; Mood, Kathleen; Daar, Ira O.
CS Regulation of Cell Growth Laboratory, National Cancer Institute-Frederick,
Frederick, MD, 21702, USA
SO Developmental Dynamics (2002), 223(2), 216-228
CODEN: DEDYEI; ISSN: 1058-8388
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The docking protein SNT1/FRS2 (**fibroblast growth factor receptor** substrate 2) is implicated in the transmission of extracellular signals from several growth factor receptors to the mitogen-activated protein (MAP) kinase signaling cascade, but its biol. function during development is not well characterized. Here, we show that the Xenopus homolog of mammalian SNT1/FRS-2 (XSNT1) plays a critical role in the appropriate formation of mesoderm-derived tissue during embryogenesis. XSNT1 has an expression pattern that is quite similar to the **fibroblast growth factor receptor**-1 (FGFR1) during Xenopus development. Ectopic expression of XSNT1 markedly enhanced the embryonic defects induced by an activated FGF receptor, and increased the MAP kinase activity as well as the expression of a mesodermal marker in response to FGF receptor signaling. A loss-of-function study using antisense XSNT1 morpholino oligonucleotides (XSNT-AS) shows severe malformation of trunk and posterior structures. Moreover, XSNT-AS disrupts muscle and notochord formation, and inhibits **FGFR**-induced MAP kinase activation. In ectodermal explants, XSNT-AS blocks **FGFR**-mediated induction of mesoderm and the accompanying elongation movements. Our results indicate that XSNT1 is a critical mediator of FGF signaling and is required for early Xenopus development.

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:866336 CAPLUS Full-text
DN 136:197236
TI **SNT**-1/FRS2α physically interacts with Laloo and mediates mesoderm induction by fibroblast growth factor
AU Hama, Joanne; Xu, Hong; Goldfarb, Mitchell; Weinstein, Daniel C.
CS Department of Pharmacology, Mount Sinai School of Medicine, New York, NY,
USA
SO Mechanisms of Development (2001), 109(2), 195-204
CODEN: MEDVE6; ISSN: 0925-4773
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Members of the fibroblast growth factor (FGF) ligand family play a crit. role in mesoderm formation in the frog Xenopus laevis. While many components of the signaling cascade triggered by FGF receptor activation have been identified, links between these intracellular factors and the receptor itself have been difficult to establish. We report here the characterization of Xenopus **SNT**-1 (FRS2α), a scaffolding protein previously identified as a mediator of FGF activity in other biol. contexts. **SNT**-1 is widely expressed during early Xenopus development, consistent with a role for this protein in mesoderm formation. Ectopic **SNT**-1 induces mesoderm in Xenopus ectodermal explants, synergizes with low levels of FGF, and is blocked by inhibition of Ras activity, suggesting that **SNT**-1 functions to transmit signals from the FGF receptor during mesoderm formation. Furthermore, dominant-inhibitory **SNT**-1 mutants inhibit mesoderm induction by FGF, suggesting that **SNT**-1 is required for this process. Expression of dominant-neg. **SNT**-1 in intact embryos blocks mesoderm formation and dramatically disrupts trunk and tail development, indicating a requirement for **SNT**-1, or a related factor inhibited by the mutant construct, during axis formation in vivo. Finally, we demonstrate that **SNT**-1 phys. assocs. with the Src-like kinase Laloo, and that **SNT**-1 activity is required for mesoderm induction by Laloo, suggesting that **SNT**-1 and

Laloo function as components of a signaling complex during mesoderm formation in the vertebrate.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:684471 CAPLUS Full-text
DN 136:64567
TI The role of **SNT** adapter proteins in FGF receptor signaling
AU Xu, Hong
CS Mount Sinai School of Medicine, New York Univ., New York, NY, USA
SO (2000) 129 pp. Avail.: UMI, Order No. DA9989860
From: Diss. Abstr. Int., B 2001, 61(10), 5163
DT Dissertation
LA English
AB Unavailable

L8 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:526106 CAPLUS Full-text
DN 135:117205
TI Modeling of the interaction of **Suc1-associated neurotrophic factor** target protein and the **fibroblast growth factor receptor** and methods of identifying modulators of the FGF receptor
IN Zhou, Ming-Ming
PA Mount Sinai School of Medicine, USA
SO PCT Int. Appl., 235 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001051521	A2	20010719	WO 2001-US821	20010110
WO 2001051521	A3	20011220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003040612	A1	20030227	US 2001-757415	20010109
EP 1246926	A2	20021009	EP 2001-900987	20010110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 2000-175867P	P	20000112		
US 2001-757415	A	20010109		
WO 2001-US821	W	20010110		

AB The present invention provides fragments of Suc1-assocd. neurotrophic factor target protein (**SNT**) and the **fibroblast growth factor receptor** (**FGFR**) which can form a binding complex that is amenable to structural anal. NMR spectroscopy. The three-dimensional structural data is also included as part of the invention. In addition, the present invention provides methodol. for related structure based rational drug design using the three-dimensional data. Mutational anal. of the interaction of the two proteins using a yeast two-hybrid system is also described. Nucleotide and amino acid sequences of the fragments are also provided.

L8 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:76625 CAPLUS Full-text
DN 134:126142
TI Letter to the Editor: 1H, 13C and 15N resonance assignments of the **SNT** PTB domain in complex with FGFR1 peptide
AU Dhalluin, Christophe; Yan, Kelley S.; Plotnikova, Olga; Zeng, Lei; Goldfarb, Mitchell P.; Zhou, Ming-Ming
CS Structural Biology Program, Department of Physiology and Biophysics, Mount Sinai School of Medicine, New York University, New York, NY, 10029-6574, USA
SO Journal of Biomolecular NMR (2000), 18(4), 371-372
CODEN: JBNME9; ISSN: 0925-2738
PB Kluwer Academic Publishers
DT Journal
LA English
AB In order to understand the detailed mol. mechanisms of the **SNT**-1 PTB (Suc1-associated neurotrophic factor target phosphotyrosine binding) domain interactions with its biol. receptors and the functional implications, the authors have undertaken NMR structural anal. of the protein in complex with FGFR1. Here the authors report the nearly complete assignments of 1H, 13C and 15N resonances for the **SNT** PTB domain complexed to a 22-residue peptide derived from the juxtamembrane region of human FGFR1.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:783390 CAPLUS Full-text
DN 134:13517
TI Structural basis of **SNT** PTB domain interactions with distinct neurotrophic receptors
AU Dhalluin, Christophe; Yan, Kelley S.; Plotnikova, Olga; Lee, Kyung W.; Zeng, Lei; Kuti, Miklos; Mujtaba, Shiraz; Goldfarb, Mitchell P.; Zhou, Ming-Ming
CS Structural Biology Program Department of Physiology and Biophysics, Mount Sinai School of Medicine, New York University, New York, NY, 10029, USA
SO Molecular Cell (2000), 6(4), 921-929
CODEN: MOCEFL; ISSN: 1097-2765
PB Cell Press
DT Journal
LA English
AB **SNT** adaptor proteins transduce activation of **fibroblast growth factor receptors** (FGFRs) and neurotrophin receptors (TRKs) to common signaling targets. The **SNT**-1 phosphotyrosine binding (PTB) domain recognizes activated TRKs at a canonical NPXpY motif and, atypically, binds to nonphosphorylated FGFRs in a region lacking tyrosine or asparagine. Here, using NMR and mutational analyses, we

show that the PTB domain utilizes distinct sets of amino acid residues to interact with FGFRs or TRKs in a mutually exclusive manner. The FGFR1 peptide wraps around the β sandwich structure of the PTB domain, and its binding is possibly regulated by conformational change of a unique C-terminal β strand in the protein. Our results suggest mechanisms by which SNTs serve as mol. switches to mediate the essential interplay between **FGFR** and TRK signaling during neuronal differentiation.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:737283 CAPLUS Full-text
DN 134:53435
TI Use of G-protein fusions to monitor integral membrane protein-protein
interactions in yeast
AU Ehrhard, Kathleen N.; Jacoby, Jorg J.; Fu, Xin-Yuan; Jahn, Reinhard;
Dohlman, Henrik G.
CS Departments of Pharmacology and Pathology, Yale University School of
Medicine, New Haven, CT, 06536, USA
SO Nature Biotechnology (2000), 18(10), 1075-1079
CODEN: NABIF9; ISSN: 1087-0156
PB Nature America Inc.
DT Journal
LA English
AB The control of protein-protein interactions is a fundamental aspect of cell regulation. Here we describe a new approach to detect the interaction of two proteins in vivo. By this method, one binding partner is an integral membrane protein whereas the other is soluble but fused to a G-protein γ-subunit. If the binding partners interact, G-protein signaling is disrupted. We demonstrate interaction between known binding partners, syntaxin 1a with neuronal Sec1 (nSec1), and the fibroblast-derived growth factor receptor 3 (FGFR3) with **SNT**-1. In addition, we describe a genetic screen to identify nSec1 mutants that are expressed normally, but are no longer able to bind to syntaxin 1a. This provides a convenient method to study interactions of integral membrane proteins, a class of mols. that has been difficult to study by existing biochem. or genetic methods.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:620865 CAPLUS Full-text
DN 131:318234
TI Inhibition of PLC-γ1 activity converts nerve growth factor from an
anti-mitogenic to a mitogenic signal in CHO cells
AU Zapf-Colby, Antje; Eichhorn, Jens; Webster, Nicholas J. G.; Olefsky,
Jerrold M.
CS Department of Medicine, Division of Endocrinology and Metabolism,
University of California, San Diego, La Jolla, CA, 92093, USA
SO Oncogene (1999), 18(35), 4908-4919
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton Press
DT Journal
LA English
AB Nerve growth factor (NGF) treatment of Chinese hamster ovary fibroblast (CHO) cells exogenously expressing 2.5 + 105 TrkA receptors (CHO/TrkA) results in inhibition of serum and insulin-like growth factor-I (IGF-I) stimulated cell proliferation in a dose-dependent manner. Furthermore, NGF does not stimulate [3H]thymidine incorporation and inhibits IGF-I mediated DNA synthesis in CHO/TrkA cells. NGF and IGF-I induce extracellular-signal regulated kinase 1 (ERK1) and ERK2 activation, but NGF is able to stimulate a higher and more sustained activation of these enzymes compared with IGF-I. Cotreatment with NGF and IGF-I yields an ERK1/2 activity profile similar to that of NGF treatment alone. While pretreatment with mitogen activated protein kinase kinase (MKK) inhibitor PD98059 (30 μM) results in 100% inhibition of IGF-I stimulated MAPK phosphorylation (IC50<1 μM), NGF mediated MAPK phosphorylation is only decreased by 50% (IC50 = 3 μM). NGF, but not IGF-I, stimulates tyrosine phosphorylation and activation of PLC-γ1 which can be inhibited in a dose-dependent manner by phosphoinositide-specific phospholipase C (PI-PLC) inhibitor U73122 (IC50 = 4 μM). Pretreatment with U73122 (IC50 = 7 μM) results in an 87% inhibition of NGF mediated MAPK phosphorylation, while cotreatment with PD98059 and U73122 results in 97% inhibition. U73122 pretreatment has no effect on NGF stimulated Akt activation. NGF, but not IGF-I, stimulates the tyrosine phosphorylation of Suc1-associated neurotrophic factor-induced tyrosine phosphorylation target (**SNT**-1)/**fibroblast growth factor receptor** substrate 2 (FRS2) which can be completely prevented by pretreatment with 10 μM U73122. Finally, inhibition of PI-PLC results in NGF's ability to stimulate DNA synthesis in the absence and presence of IGF-I.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:484205 CAPLUS Full-text
DN 129:198122
TI Novel recognition motif on **fibroblast growth factor receptor** mediates direct association and activation of **SNT** adapter proteins
AU Xu, Hong; Lee, Kyung W.; Goldfarb, Mitchell
CS Brookdale Center for Developmental and Molecular Biology, Mount Sinai
School of Medicine, New York, NY, 10029, USA
SO Journal of Biological Chemistry (1998), 273(29), 17987-17990
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Fibroblast growth factors (FGFs) stimulate tyrosine phosphorylation of a membrane-anchored adapter protein, FRS2/**SNT**-1, promoting its association with Shp-2 tyrosine phosphatase and upstream activators of Ras. Using the yeast two-hybrid protein-protein interaction assay, we show that FRS2/**SNT**-1 and a newly isolated **SNT**-2 protein directly bind to FGF receptor-1 (**FGFR**-1). A juxtamembrane segment of **FGFR**-1 and the phosphotyrosine-binding domain of SNTs are both necessary and sufficient for interaction in yeast and in vitro, and **FGFR**-mediated **SNT** tyrosine phosphorylation in vivo requires these segments of receptor and **SNT.** Our findings establish SNTs as direct protein links between **FGFR**-1 and multiple downstream pathways. The **SNT** binding motif of **FGFR**-1 is distinct from previously described phosphotyrosine- binding domain recognition motifs, lacking both tyrosine and asparagine residues.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR

THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:420998 CAPLUS Full-text
DN 129:131437
TI Identification of the cytoplasmic regions of fibroblast growth factor
(FGF) receptor 1 which play important roles in induction of neurite
outgrowth in PC12 cells by FGF-1
AU Lin, Hsien-Yi; Xu, Jingsong; Ischenko, Irene; Ornitz, David M.; Halegoua,
Simon; Hayman, Michael J.
CS Institute of Cell and Developmental Biology, Graduate Program in Molecular
Biology and Biochemistry, Stony Brook, NY, 11794, USA
SO Molecular and Cellular Biology (1998), 18(7), 3762-3770
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB Fibroblast growth factor 1 (FGF-1) induces neurite outgrowth in PC12 cells. Recently, the authors have shown that the FGF receptor 1 (**FGFR**-1) is much more potent than **FGFR**-3 in induction of neurite outgrowth. To identify the cytoplasmic regions of **FGFR** -1 that are responsible for the induction of neurite outgrowth in PC12 cells, the authors took advantage of this difference and prepared receptor chimeras containing different regions of the **FGFR**-1 introduced into the **FGFR**-3 protein. The chimeric receptors were introduced into FGF-nonresponsive variant PC12 cells (fnr-PC12 cells), and their ability to mediate FGF-stimulated neurite outgrowth of the cells was assessed. The juxtamembrane (JM) and C-terminal (COOH) regions of **FGFR**-1 were identified as conferring robust and moderate abilities, resp., for induction of neurite outgrowth to **FGFR**-3. Anal. of FGF-stimulated activation of signal transduction revealed that the JM region of **FGFR**-1 conferred strong and sustained tyrosine phosphorylation of several cellular proteins and activation of MAP kinase. The **SNT**/FRS2 protein was demonstrated to be one of the cellular substrates preferentially phosphorylated by chimeras containing the JM domain of **FGFR**-1. **SNT**/FRS2 links FGF signaling to the MAP kinase pathway. Thus, the ability of **FGFR**-1 JM domain chimeras to induce strong sustained phosphorylation of this protein would explain the ability of these chimeras to activate MAP kinase and hence neurite outgrowth. The role of the COOH region of **FGFR**-1 in induction of neurite outgrowth involved the tyrosine residue at amino acid position 764, a site required for phospholipase C gamma binding and activation, whereas the JM region functioned primarily through a non-phosphotyrosine- dependent mechanism. In contrast, assessment of the chimeras in the pre-B lymphoid cell line BaF3 for FGF-1-induced mitogenesis revealed that the JM region did not play a role in this cell type. These data indicate that **FGFR** signaling can be regulated at the level of intracellular interactions and that signaling pathways for neurite outgrowth and mitogenesis use different regions of the **FGFR.**
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:363011 CAPLUS Full-text
DN 127:104555
TI A lipid-anchored Grb2-binding protein that links FGF-receptor activation
to the Ras/MAPK signaling pathway
AU Kouhara, H.; Hadari, Y. R.; Spivak-Kroizman, T.; Schilling, J.; Bar-Sagi,
D.; Lax, I.; Schlessinger, J.
CS Department Pharmacology, New York University Medical Center, New, NY,
10016, USA
SO Cell (Cambridge, Massachusetts) (1997), 89(5), 693-702
CODEN: CELLB5; ISSN: 0092-8674
PB Cell Press
DT Journal
LA English
AB Activation of the Ras/MAPK signaling cascade is essential for growth factor-induced cell proliferation and differentiation. The authors describe the purification, cloning, and characterization of a novel protein, designated FRS2, that is tyrosine phosphorylated and binds to Grb2/Sos in response to FGF or NGF stimulation. The authors find that FRS2 is myristylated and that this modification is essential for membrane localization, tyrosine phosphorylation, Grb2/Sos recruitment, and MAPK activation. FRS2 functions as a lipid-anchored docking protein that targets signaling mols. to the plasma membrane in response to FGF stimulation to link receptor activation with the MAPK and other signaling pathways essential for cell growth and differentiation. Finally, the authors demonstrate that FRS2 is closely related and probably identical to **SNT**, the long-sought target of FGF and NGF receptors.

=> d his

(FILE 'HOME' ENTERED AT 14:38:03 ON 07 SEP 2004)

FILE 'CAPLUS' ENTERED AT 14:38:12 ON 07 SEP 2004
L1 2 S (SUC1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB
L2 139 S SNT/BI,AB
L3 0 S (SUC(W)1(W)ASSOCIATED(W)NEUROTROPHIC(W)FACTOR#)/BI,AB
L4 139 S L1 OR L2 OR L3
L5 3240 S (FIBROBLAST(W)GROWTH(W)FACTOR(W)RECEPTOR#)/BI,AB
L6 1018 S FGFR/BI,AB
L7 3397 S L5 OR L6
L8 16 S L4 AND L7

=> log y

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STN INTERNATIONAL LOGOFF AT 14:41:20 ON 07 SEP 2004

L Number	Hits	Search Text	DB	Time stamp
2	2	suc1 adj associated adj neurotrophic adj factor$1	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:28
3	0		USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:28
4	1	suc adj "1" adj associated adj neurotrophic adj factor$1	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:28
5	317	snt	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:28
6	2869	fibroblast adj growth adj factor adj receptor$1	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:29
7	901	fgfr	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:29
8	3	(suc1 adj associated adj neurotrophic adj factor$1) or (suc adj "1" adj associated adj neurotrophic adj factor$1)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:29
9	3338	(fibroblast adj growth adj factor adj receptor$1) or fgfr	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:29
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11	21	snt and ((fibroblast adj growth adj factor adj receptor$1) or fgfr)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:30

12	21	(((suc1 adj associated adj neurotrophic adj factor$1) or (suc adj "1" adj associated adj neurotrophic adj factor$1)) and ((fibroblast adj growth adj factor adj receptor$1) or fgfr)) or (snt and ((fibroblast adj growth adj factor adj receptor$1) or fgfr))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:30
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14	25739	"3" adj dimension$	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:31
15	139299	3d	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:31
16	139299	"3d"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:31
17	49653	"3" adj "d"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:31
18	49653	"3" adj d	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:31
19	443036	(three adj dimension$) or ("3" adj dimension$) or 3d or "3d" or ("3" adj "d") or ("3" adj d)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:31
20	16	((((suc1 adj associated adj neurotrophic adj factor$1) or (suc adj "1" adj associated adj neurotrophic adj factor$1)) and ((fibroblast adj growth adj factor adj receptor$1) or fgfr)) or (snt and ((fibroblast adj growth adj factor adj receptor$1) or fgfr))) and ((three adj dimension$) or ("3" adj dimension$) or 3d or "3d" or ("3" adj "d") or ("3" adj d))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2004/09/07 14:32